

Attorney Docket No.: 4341.224-US  
Application No.: 10/620,651  
Filed: July 16, 2003  
Applicants: Jan Markussen et al.  
Via Facsimile : 571-273-8300

### **REMARKS/ARGUMENTS**

Claims 1-26, 47-94, and 117-136 will be pending following entry of this Amendment.

### **OBVIOUSNESS-TYPE DOUBLE PATENTING REJECTION**

A. The rejection of claims 1-136 (now 1-26, 47-94, and 117-136) under the non-statutory doctrine of obviousness-type double patenting as being unpatentable over claims 1-95 of US Patent No. 5,750,497 and claims 1-115 of US Patent No. 6,011,007 is respectfully traversed.

US 5,750,497 (US '497) and US 6,011,007 (US '007) are from the same patent family (Applicants note that a third patent, US 6,869,930, has issued in this family with claims to insulin derivatives wherein the  $\epsilon$ -amino group Lys<sup>B29</sup> is substituted with a lipophilic substituent having at least 6 carbon atoms).

The claims of US '497 are to insulin derivatives wherein the  $\epsilon$ -amino group Lys<sup>B29</sup> is substituted with an acyl group having at least 10 carbon atoms and the claims of US '007 are to insulin derivatives wherein the  $\epsilon$ -amino group Lys<sup>B29</sup> is substituted with a lipophilic substituent having at least 10 carbon atoms. In contrast, the B29 position of the presently claimed insulin derivative is Xaa, which is either absent or any codable amino acid except Cys. There is no recitation in the presently claimed invention of Lys<sup>B29</sup> having an acyl-substituted  $\epsilon$ -amino group or an  $\epsilon$ -amino group substituted with a lipophilic substituent.

Attorney Docket No.: 4341.224-US  
Application No.: 10/620,651  
Filed: July 16, 2003  
Applicants: Jan Markussen et al.  
Via Facsimile : 571-273-8300

Furthermore, the presently claimed invention requires that the B-chain have either 1) an N-terminal lipophilic group attached via the N-terminal amine or 2) a C-terminal lipophilic group attached via the C-terminal carboxyl group and Applicants submit that these presently claimed N-terminal or C-terminal lipophilic groups are not obvious variants of the Lys<sup>B29</sup> ε-amino group acyl and lipophilic substituents of US '497 and US '007 respectively. In particular, the N-terminal substituent in the present claims is located 28 amino acids away from the acyl group of US '497 and the lipophilic substituent of US '007 respectively while the C-terminal substituent in the present claims is attached to the carboxyl group of the C-terminal amino acid of the B-chain whereas the acyl and lipophilic substituents of US '497 and US '007 respectively are attached to the Lys<sup>B29</sup> ε-amino group. In view of these distinct differences, Applicants submit that the presently claimed invention is not obvious over claims 1-95 of US Patent No. 5,750,497 or claims 1-115 of US Patent No. 6,011,007. Withdrawal of these rejections is respectfully requested.

B. Claims 1-136 (now 1-26, 47-94, and 117-136) were rejected under the non-statutory doctrine of obviousness-type double patenting as being unpatentable over claims 1-23 of US Patent No. 6,251,856 and claims 1-23 of US Patent No. 6,620,780.

In response, Applicants respectfully submit terminal disclaimers (2) over these patents to obviate these double patenting rejections. Withdrawal of these two obviousness-type double patenting rejections is respectfully requested.

Attorney Docket No.: 4341.224-US  
Application No.: 10/620,651  
Filed: July 16, 2003  
Applicants: Jan Markussen et al.  
Via Facsimile : 571-273-8300

### **REJECTION OF THE CLAIMS UNDER 35 USC 112**

The rejection of claims 1, 12, 27, 47, 69, 95, and 117 (now 1, 12, 47, 69, and 117) under §112, 1<sup>st</sup> paragraph, as failing to comply with the written description requirement has been obviated by appropriate amendment.

The phrase "a derivative of a parent insulin having the following sequence" has been replaced by "an insulin derivative..." as suggested by the Examiner. Withdrawal of this rejection is respectfully requested.

The rejection of claim 12 under §112, 1<sup>st</sup> paragraph, as failing to comply with the written description requirement has been obviated by appropriate amendment.

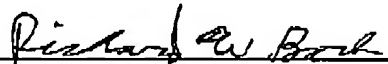
Claim 12 has been amended to recite that the hexameric complex is a hexameric insulin complex that comprises at least one insulin derivative of the present invention. Thus, the hexamer is six insulins, at least one of which is an insulin derivative of the present invention. Applicants submit that this amendment clarifies the claimed subject matter of claim 12 and respectfully request withdrawal of the §112, 1<sup>st</sup> paragraph, rejection.

Attorney Docket No.: 4341.224-US  
Application No.: 10/620,651  
Filed: July 16, 2003  
Applicants: Jan Markussen et al.  
Via Facsimile : 571-273-8300

It is believed that the claims as presented are in condition for allowance, and a determination to that effect is earnestly solicited.

Respectfully submitted,

Date: November 27, 2006

  
Richard W. Bork, Reg. No. 36,459  
Novo Nordisk, Inc.  
100 College Road West  
Princeton, NJ 08540  
(609) 987-5800

CUSTOMER NUMBER  
23650  
PATENT TRADEMARK OFFICE